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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,144	07/09/2003	Antje Von Schaewen	310257-1101	5104

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EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 02/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/615,144	SCHAEWEN, ANTJE VON	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U:S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3 and 31-48* is/are pending in the application.

4a) Of the above claim(s) *35-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/591,466.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/9/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on November 15, 2005 from William H. Benz, the election with traverse of group I, claims 2-3 and 31-34 as they relate to SEQ ID NO:3 is acknowledged. The Applicant traverses on the grounds that examination of SEQ ID NOs: 1, 3, and 5 together would not represent an undue burden as they all share the same function. This argument is not persuasive because each of these sequences would require a separate sequence search which is a burden on PTO resources. The restriction requirement is maintained and is made final. Claims 2-3 and 31-48 are pending; claims 35-48 are withdrawn from consideration.

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the following:

- Page 18 lines 25 (AWRHPQFGG) and lines 26 and 34 (IEGR)
- Figure 2, cDNA sequence and amino acid sequence
- Figure 3B 3 different amino acid sequences

- Page 31 lines 22-24, 2 primer sequences and line 36 amino acid sequence
- Page 34 lines 26-28, 2 primer sequences
- Page 36, lines 4-6, 2 primer sequences.

If these sequences do not already have sequence ID numbers assigned to them, then an amendment to the sequence listing will be required as well. There must not be any new matter submitted, therefore it is important to be careful to include only the sequences that are already disclosed in the current specification and figures.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

Information Disclosure Statement

3. The information disclosure statement filed July 9, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The majority of the documents were contained in the parent

application, 09/591,466, and were considered. However, there were 5 missing documents and one document that was listed on the 1449 with an incorrect title and publication year. The 5 missing documents were:

- Chemical Abstracts 119: 245692f
- Chemical Abstracts 120: 294245s
- EML-Genbank AC B24856
- EML-Genbank AC AC000098
- Altmann et al. PNAS (1990) Vol. 87, pp. 1913-1916

The document listed with an incorrect title and publication year was Damm, B. et al. (1998) MGG Vol. 213, pp. 15-20.

4. The listing of references in the specification in pages 38-43 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: - - Method for reduction of N-acetyl glucosaminyl transferase activity utilizing antisense GnTI from tobacco - - .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2-3 and 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

Claim 31 recites "cultivating a transgenic plant, parts of transgenic plants, or transformed plant cells" which is indefinite. How does one cultivate a part of a plant? How does one cultivate a plant cell? Cultivate implies planting. Does the Applicant mean culturing?

Claim 31 recites "transformed with an antisense construct or a sense construct, comprising an antisense DNA or a sense DNA". It is unclear what is

encompassed by these constructs. Does the sense construct comprise an antisense DNA? Or does the antisense construct comprise a sense DNA?

7. Claims 2-3 and 31-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2-3 and 31-34 are drawn to a method utilizing a gene or a cDNA for plant N-acetyl glucosaminyl transferase I (GnTI) or a part thereof for elimination or reduction of the activity of said N-acetyl glucosaminyl transferase (GNT).

The essential feature of the invention is the elimination or reduction of GNT activity. The claims are directed to a method utilizing a genus of molecules encompassing sense and antisense constructs comprising sequences from any gene or any cDNA for a plant GnTI or a part thereof; thus the genus of molecules is broad and includes virtually any nucleic acid. There has only been one species reduced to practice; an antisense construct comprising the full-length GnTI cDNA from potato (see page 30 lines 4-6, and page 34, in particular). The specification describes no sense constructs that eliminate or reduce GNT activity, and there have been no parts of a plant GnTI cDNA that have been reduced to practice. Given the

multitudes of molecules encompassed by the claims, the one species reduced to practice is not representative of this large genus.

Furthermore, the specification does not describe any specific structures or motifs that are sufficient for the function of reducing or eliminating GNT activity. The specification has described the complete potato GnTI cDNA and has reduced to practice an antisense construct comprising the full-length potato cDNA. The specification has described the complete cDNA of SEQ ID NO:3, but no subsequences or parts of SEQ ID NO:3 have been described. Without a description of specific subsequences or motifs within SEQ ID NO:3 that are known to be effective for reducing or eliminating GNT activity, there is no structure/function relationship established. Given the large genus of molecules encompassed by the claims, and given only one species reduced to practice and no further description of subsequences or motifs associated with the desired function, the written description requirement has not been met.

8. Claims 2-3 and 31-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising transforming a tobacco or potato plant with a construct comprising SEQ ID NO:3 in the antisense orientation relative to a promoter that functions in plants, does not reasonably provide enablement for a method comprising transforming any plant with an antisense or sense construct comprising any plant GnTI gene or cDNA or

part thereof with or without an additional regulatory sequence for its transcription. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 2-3 and 31-34 are broadly drawn to a method for elimination or reduction of the activity of GNT, comprising transforming a plant with an antisense or a sense construct comprising a gene or cDNA for a plant GnTI or a part thereof, wherein the construct optionally contains additional regulatory sequences for the transcription of the sense or antisense DNA.

The nature of the invention is the generation of transgenic potato and tobacco plants with reduced GNT activity which were transformed with antisense constructs comprising the full-length GnTI cDNA from potato.

At the time of filing, the prior art was very limited regarding plant GNT enzymes. One Arabidopsis mutant which lacked GNT activity was known in the art (Schaewen, A.v., et al. (1993) Plant Physiology, Vol. 102, pp. 1109-1118). The amino acid sequences of GNT enzymes from plants and the nucleic acid sequences of the genes encoding the plant enzymes were not known in the art. The instant application discloses the amino acid sequences of 3 GnTI enzymes; one from potato, one from tobacco, and one from Arabidopsis (see figure 3B, in particular) and the nucleic acid sequences of the cDNAs encoding these enzymes; SEQ ID NOs: 1, 3, and 5, respectively, (see pages 32-33, in particular). The tobacco cDNA (SEQ ID

NO:3) shares 72% homology with the potato cDNA (SEQ ID NO:1) and 44% homology with the Arabidopsis gene (SEQ ID NO:5), (see results of STIC sequence search, in particular). The specification discloses that an antisense construct comprising the full-length GnTI cDNA from potato was used to generate transgenic potato and tobacco plants, and the resulting transformants were disclosed to have reduced GnTI activity resulting in a reduction of complex glycoprotein modification (see page 35 lines 22-33, page 30 lines 4-6, and Figure 5, in particular).

The specification does not disclose any working examples of co-suppression to reduce GNT activity by transforming a plant with a sense construct. On page 17, lines 13-45, the specification teaches that transgenic plants can be made with increased GNT activity by transforming with a sense construct, and on page 33 in lines 16-35, the specification provides a working example wherein functional GNT enzyme is produced by Arabidopsis that is transformed with a sense construct. One would predict that GNT activity would be elevated by transformation with a sense construct rather than being reduced or eliminated.

In addition, the specification does not disclose any "parts" of genes or cDNAs that are used for reducing or eliminating GNT activity. The only working example utilizes an antisense construct with the full-length potato GnTI cDNA. The specification has not provided any guidance with regard to what regions of the cDNA would be required to generate an effective antisense construct.

Furthermore, claim 32 recites "wherein the antisense or sense construct optionally contains additional regulatory sequences for the transcription of the respective antisense or sense DNA". One of skill in the art would be able to make a construct without a promoter, but the method would not work without a promoter that functions in plants. The Applicant has not taught any constructs lacking a promoter that are effective for elimination or reduction of GNT activity.

Additionally, the claims encompass the use of antisense or co-suppression in multiple plant species. Antisense suppression of gene expression is highly unpredictable, and the prior art suggests that success depends on the % identity between the sequence of the antisense construct and the target gene sequence (see Elomaa et al. (1996) Molecular Breeding, Vol. 2, pp. 41-50; paragraph bridging pages 47-48, in particular). Klee et al. teach that antisense genes would probably be species-specific, and therefore a different antisense gene would be required for each species of plant desired to be transformed (see US Patent # 5,702,933, issued Dec. 30, 1997, column 1 lines 60-65, in particular). In the instant application, the Applicants teach that "by the use of heterologous GntI gene sequences an efficient reduction of endogenous complex glycoprotein modification in plants by means of antisense or sense suppression, respectively, probably cannot be achieved" (see page 5 lines 15-19, in particular). Because the antisense construct utilizing the potato cDNA was effective in both potato and tobacco plants, it is reasonable to expect that an antisense construct utilizing the full-length tobacco cDNA (SEQ ID NO:3) would

be effective in both tobacco and potato plants. The outcome in any other plant species would be highly unpredictable.

In cases where the target gene is a member of a gene family, there is an additional amount of unpredictability. The instant application discloses that potatoes have at least two genes encoding GNT (see page 21 lines 4-6, in particular), and it is unknown how many other plants may have multi-gene families encoding different isoforms of GNT. In one study, Colliver et al. taught that antisense of members of a gene family is highly unpredictable (PMB (1997) Vol. 35, pp. 509-522). Colliver et al. showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with increased levels of chalcone synthase transcripts due to increased transcription of other members of the gene family (see page 519 left column paragraph 2, in particular).

Because of the sequence variability between the different genes in different species of plants and because of the inconsistent results taught in the prior art, there is a high degree of unpredictability in the use of antisense or co-suppression to inhibit the expression of different genes. Given the breadth of the claims encompassing the use of any gene or cDNA or part thereof in antisense or sense constructs to transform any plant, and given that there is only one working construct that functions in only potato and tobacco and given a high degree of unpredictability as discussed above, it would require undue experimentation on the part of one of skill in the art to make and use the invention as claimed.

9. Claims 2-3 and 31-34 are free of the prior art because the prior art does not teach or fairly suggest a method for eliminating or reducing GNT activity in a plant using antisense or cosuppression.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ANNE KUBELIK, PH.D.
PRIMARY EXAMINER

CKW
Feb. 1, 2006